

Remarks

Claims 1, 4, 11, 12, 15, 16, 18, 70, and 73-79 are pending. Applicants hereby amend claims 1, 18, and 70 and add new claims 73-79.

These amendments for claims 1, 18, and 70 are supported throughout Applicants' specification. As noted in more detail below, the present amendments refine the claims grammatically and with regard to punctuation without affecting scope. New claims 73-79 are supported throughout Applicants' specification, including but not limited to the exemplified compounds described at page 66 *et seq.*

Restriction

Applicants thank the Examiner for his assistance in resolving the issues concerning the restriction. Applicants elect Group I, compounds of Formulae 1 or 2, where k is 1; p is 1; when m is 1, n is 0; when m is 0, n is 1; Ar is optionally substituted pyridinyl. Applicants appreciate the Examiner's efforts with regard to Figure 1 of the Office Action. The proposed amendments address each of the Examiner's concerns with regard to the restriction.

Notably, claim 11 is still pending in the application. The Office Action notes claim 11 as withdrawn. To the contrary, claim 11 remains within the elected Group I. Applicants cancel claims 13 and 17 as redundant over the amendments made to satisfy the restriction requirement. Applicants request confirmation from the Examiner.

Claim 18 is hereby amended further based upon the definitions of "k" and "p" to remove non-elected subject matter. More specifically, Applicants remove three general formulae from the list based upon the location of the nitrogen atom relative to the bridge. Applicants request confirmation from the Examiner.

35 USC §112, Second Paragraph

The Examiner rejected claim 1 under 35 USC §112, second paragraph based on the recitation of such phrases as "such as" and "the like." See the Office Action, page 8.

Applicants believe the present amendments address the Examiner's concerns regarding §112, second paragraph. With regard to the revision associated with the phrase regarding stereoisomerism, Applicants note that the compounds of the present invention include chiral centers and the scope of the present invention includes racemates as well as substantially enantiopure compounds. Applicants remove the language from the claims, however, since the language appears superfluous and those

skilled in the art will recognize the scope of the claimed invention includes this subject matter.

Accordingly, all asserted bases for rejection are properly rendered moot and Applicants respectfully request that the rejection be withdrawn.

35 USC §112, First Paragraph

The Examiner rejected claims 1, 4, 12, 13, 15-18, and 70 under 35 USC §112, first paragraph, as non-enabling for the breadth of claim scope. See the Office Action, page 9. For ease of reference regarding the Examiner's rejections based upon §112, first paragraph, Applicants address the Examiner's rejections in the order provided in the Office Action.

Positional Isomers

Applicants appreciate the Examiner's thorough review of the specification. The cause for the Examiner's rejection likely lies in nomenclature, rather than substance. For example, with regard to the positional isomers, IA and IC as compared to IB and ID, the chemistry exemplified in Example 18 fully supports the relevant claim scope. Thus, the 2-(pyridine-3-yl)-7-azabicyclo[3.3.1]non-2-ene compound that the Examiner uses to argue the lack of enablement is, in fact, the 6-(pyridine-3-yl)-3-azabicyclo[3.3.1]non-6-ene compound whose synthesis is exemplified specifically in Example 18. Applicants agree that the wide variety of acceptable nomenclature rules for compounds of this class provide the potential for initial disagreement. In light of this clarification, however, Applicants request withdrawal of this §112, first paragraph rejection.

Substituents on the pyridine ("Ar")

As currently claimed, "Ar" is defined as pyridinyl with one or more optional substituents "Z." Applicants disagree with the Examiner's rejection regarding the allowable support for "Z" as substituted from the pyridine ring. The synthetic schemes and specific examples provide ample support for the relevant claim scope. For instance, and not meant to limit, Example 20 and 21 provide specific exemplification for compounds outside the Examiner's proposed limits. More specifically, Example 20 and 21 exemplify an aryl and an aryloxy substitution, neither of which appears in the list proposed by the Examiner on page 9, numbered paragraph 5, of the Office Action. The list provided in the claim is well within the purview of one of ordinary skill based upon the synthetic examples provided in the present specification. Applicants respectfully request withdrawal of this §112, first paragraph rejection.

Definition of "R"

Again, Applicants disagree with the assertions made in the Office Action. Nevertheless, in order to advance prosecution, Applicants amend the claims as requested. Applicants believe the rejection is now moot and request withdrawal.

Substituents on the azabicyclic ring (definition of "j")

Applicants disagree with the Examiner's rejection regarding the nature of "Z" as substituted from the azabicyclic ring. The Examiner's expertise in synthetic chemistry is noted and greatly appreciated. Because of the Examiner's high level of skill, beyond ordinary skill, the Examiner will readily appreciate that the exemplified chemistry is not the only means of making the claimed compounds. As those of ordinary skill will note, the 3-azabicyclo[3.3.1]nonan-7-one is not a "necessary" intermediate, but simply one used to exemplify the synthesis in the present specification. Other means of synthesis may be performed and are readily available. Notably, those skilled in the art will appreciate that substituent groups, such as alkyl groups, survive both Birch reduction and LiAlH₄ reductions. Also, ketones readily serve as entry, by a variety of well-known chemistries, to substituted compounds, for example alkyl and halo substitutions. Applicants respectfully request withdrawal of this §112, first paragraph rejection.

Claim 70

Applicants disagree with the Examiner's rejection regarding claim 70 and reference to an antineoplastic agent and a VEGF-inhibitor. While Applicants agree that the scope of these terms is broad, breadth does not necessarily equate with lack of enablement. Rather, the standard for enablement is whether the experimentation needed to practice the invention is undue or unreasonable. Even though the statute does not use the phrase "undue experimentation," this is the standard upon which enablement is measured.

The specification need not teach, and preferably omits, what is well known in the art. In this case, antineoplastic agents and VEG-F inhibitors are known and disclosed in the prior art. Further, experiments, such as binding assays, are known and disclosed in the prior art. Those skilled in the art may determine readily whether an agent is an antineoplastic agent. Likewise, those skilled in the art may determine readily whether an agent is a VEG-F inhibitor. The fact that experimentation is complex is not dispositive that the experimentation is undue, especially if those skilled in the art typically engage in such experimentation. Notably, in the case cited by the Examiner, *In re Wands*, the Patentee did provide an enabling disclosure based, in part, on the fact that all of the

methods needed to practice the invention were well known. As is the case here, the ability to determine the characteristic of any compound or agent as having a particular affinity for a target involves methods well-known to those in the art. As one example, Applicants cited cisplatin as a well-known antineoplastic agent. Cisplatin (otherwise known as cisplatinum or cis-diamminedichloroplatinum(II) (CDDP)) is a platinum-based chemotherapy drug used to treat various types of cancers. The known uses include sarcomas, some carcinomas, such as small cell lung cancer, and ovarian cancer, lymphomas, and germ cell tumors. Applicants believe that cisplatin was the first member of its class, but the class now also includes other agents such as carboplatin and oxaliplatin. For further information, Applicants direct the Examiner to the *Physician's Desk Reference*, for example, the Product Category Index and the heading "ANTINEOPLASTICS" contained therein. Applicants respectfully request withdrawal of this §112, first paragraph rejection.

Applicants believe that this Response addresses each of the points made in the Office Action. As such, the claims are allowable and such action is requested. Should the Examiner have any additional issue, he is encouraged to telephone the undersigned for expeditious handling.

Respectfully submitted,

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